year changes in the ratio were beneficially affected by lifestyle factors, but only to a modest degree. It is concerning that obesity at baseline contributes to a significant worsening of the ratio whereas a report of exercise only slightly improves the ratio.

1202-88 Cholesterol Screening of Adults in the US: Role of Socio-demographic Factors

Christopher R. Bartalos, Chao Sun, Jacqueline S. Marinac, *The University of Health Sciences, Kansas City, Missouri, Medical Center of Independence, Independence, Missouri.*

Background: The National Cholesterol Education Program (NCEP) II & Expert Panel Adult Treatment Panel III (ATPIII) guidelines recommend a cholesterol screen every 5 years for all adults ≥20 yrs age. No information regarding the role of socio-demographic factors on US adult cholesterol screening has been published.
Methods and Results: Data were extracted from the 1999 CDC Behavioral Risk Factor Surveillance System (BRFSS) survey. The BRFSS telephone surveyed 159,000 US adults regarding cholesterol screening within the last 5 years. Data were stratified by age, gender, ethnicity, income, education, level of insurance and the ability to afford health care. Overall 69% adults were screened within the last 5 yrs, which is below the Healthy People 2000/2010 goals of 75% & 80% respectively. However 85% adults >65 years were screened. Adults aged ≥45 years were 3.7 times more likely to receive cholesterol screening. Those with health insurance were 2.4 times more likely to receive screening. High school graduates or those with some college were 1.5 times more likely to be screened. Women were 1.2 times more likely to be screened. Those with an income ≥$20K/yr were 1.4 times more likely to receive screening. The socio-demographic variables had a compounding influence on cholesterol screening. For example, the individual <45 yrs age, who was less educated, with a lower economic status and had no health insurance was the least likely to report having received cholesterol screening within the last 5 years (29%).
Conclusion: Socio-demographic factors play an important role in cholesterol screening. This information may be used for targeted future cholesterol screening interventions.

1202-89 Contemporary Awareness and Understanding of Cholesterol as a Risk Factor: Results of an American Heart Association National Survey

Ira S. Nash, Lori Mosca, Roger S. Blumenthal, Michael Davidson, Sidney C. Smith, Richard C. Pasternak, *Mount Sinai School of Medicine, New York, New York.*

Public awareness and understanding of risk factors for atherosclerotic vascular disease are essential for successful primary and secondary prevention. The American Heart Association conducted a national telephone survey to assess public knowledge of the link between cholesterol and heart disease and the specifics of cholesterol management in April 2001. A national probability sample of 1114 adults age 40 years and older was interviewed by trained personnel using a structured format. Good regional distribution was achieved; 29% of respondents were over age 65, 56% were women and 87% were white. Most (55%) were employed and of those, 70% identified themselves as white-collar workers. Over 90% had at least a high school education and over 30% completed college. Although 91% stated that it was "important to them personally to have a healthy cholesterol level" (77% extremely or very important), 51% did not know their own level. Only 40% were aware of national guidelines for cholesterol management, and 52% could not identify the correct desirable total cholesterol level for a healthy adult. More people selected HDL than LDL as the most important lipid fraction to control (22% vs 16%). When asked what sources of information they rely on the most, 67% identified physicians and 13% stated magazines were their principal sources, while only 4% rely primarily on the internet.
Conclusion: public awareness of the importance of cholesterol as a risk factor for cardiovascular disease is high, but specific knowledge of cholesterol management is poor. Patients overwhelmingly identify physicians as their primary source of information. Therefore, physicians have an important opportunity to improve public understanding and management of lipid abnormalities.

1202-90 Lowering LDL Cholesterol With Simvastatin, an HMG-CoA Reductase Inhibitor, Does Not Affect Luteal Function in Women

Nanette Santoro, Diane Plotkin, Yale Mitchel, Joanne Waldstreicher, Minzhi Liu, *Albert Einstein College of Medicine, Bronx, New York, Merck Research Laboratories, Rahway, New Jersey.*

Background: Cholesterol is the precursor of all steroid hormones, therefore cholesterol-reducing drugs could theoretically disrupt gonadal function in premenopausal women.
Methods: This double-blind, randomized, placebo-controlled study was conducted to evaluate the effects of simvastatin treatment in premenopausal women. Normally cycling women (n=86) with elevated baseline LDL cholesterol (LDL-C) levels (130-250 mg/dL) were studied over six menstrual cycles. At the end of the screening phase (cycle #1), participants received placebo for the second menstrual cycle, and subsequently were randomized to receive either placebo (n=44) or simvastatin 40 mg/day (n=42) for the next four menstrual cycles (cycle #3-6). The second and sixth menstrual cycles were considered baseline and treatment cycles, respectively. Participants kept a menstrual diary throughout the study, recording onset and duration of bleeding, and provided daily first-void urine samples (cycles #2 and 6). Urine samples were assayed for lutenizing hormone (LH) and pregnanediol glucuronide (PdG), the chief urinary metabolite of progesterone. The primary endpoint was change in luteal phase duration as defined by the day of the urinary LH peak to the day preceding the onset of menstruation. The primary hypothesis was that there would not be a clinically significant decrease (4 days) in luteal phase duration between the treatment groups.
Results: Simvastatin lowered LDL-C and triglycerides by 34.3 (p<0.001) and 14.7% (p<0.001), respectively, and raised high-density lipoprotein cholesterol by 4.9% (p<0.050). Simvastatin treatment had no clinically relevant effect on luteal phase duration, peak PdG concentration, or integrated luteal phase PdG concentration compared to the placebo group. Furthermore, the number of women experiencing anovulatory cycles or abnormal cycle lengths did not differ between the treatment groups.
Conclusion: Treatment with simvastatin 40 mg/day was safe and effective at lowering LDL-C and did not adversely affect the hypothalamic-pituitary-gonadal axis in premenopausal women.

ORAL CONTRIBUTIONS

873 Venous Thromboembolism: Prevention and Treatment

Tuesday, March 19, 2002, 4:00 p.m.-5:00 p.m.
Georgia World Congress Center, Room 255W

4:00 p.m.

873-1 Lack of Association of Celecoxib With an Increased Risk of Thromboembolic Events

Gerald Faich, I. E. Allen, S. D. Ross, James B. Lefkowith, *Pharmaceutical Safety Assessments, Inc., Narberth, Pennsylvania, Metaworks, Inc., Medford, Massachusetts.*

Background: It has been hypothesized that COX-2 specific inhibitors may increase the risk of cardiovascular (CV) thromboembolic events because of their inhibition of vascular prostacyclin synthesis and lack of an effect on platelet aggregation.
Methods: Data from the celecoxib clinical trial database were analyzed to determine the incidence of serious thromboembolic events (cardiac, cerebrovascular and peripheral vascular events) using a methodology derived from a recent FDA cardiorenal review (NDA 21-042, S-007). Since aspirin use for CV prophylaxis (<325 mg/d) was permitted, the analysis was performed for all patients and patients not taking aspirin.
Results: The incidence rates, patient exposure and relative risk (RR) for the long term safety trial CLASS (duration 12-15 mo.), 15 controlled arthritis trials (durations 3-6 mo.) and the open label long term safety trial (duration 24-36 mo.) for celecoxib and NSAIDs (naproxen, diclofenac, ibuprofen) are shown in the following table (unadjusted for differences in study demographics and cardiac risk factors).
Conclusion: These data suggest that celecoxib is not associated with an increased incidence of serious thromboembolic events when compared to NSAIDs and thus do not support the hypothesis of a class effect of COX-2 specific inhibitors on CV events.
Disclosure: Sponsored by Pharmacia Corporation and Pfizer Inc.

	Celecoxib	NSAIDs	RR (95% CI)
CLASS	Rate/100 pt-yrs (total patient exposure)		
All Patients	2.24 (2,320)	2.22 (2,203)	1.01 (0.67-1.52)
Non-ASA	1.39 (1,804)	1.34 (1,715)	1.03 (0.56-1.91)
Arthritis Trials			
All	1.41 (2,845)	1.59 (1,445)	0.88 (0.52-1.55)
Non-ASA	0.73 (2,587)	1.21 (1,325)	0.61 (0.30-1.26)
Open Label Trial			
All	1.37 (7,024)	--	--
Non-ASA	0.80 (5,720)	--	--
Combined Trials (CLASS, Arthritis, Open Label)			
All	1.59 (11,693)	1.97 (3,648)	0.81 (0.61-1.07)
Non-ASA	0.92 (9,677)	1.28 (3,040)	0.72 (0.49-1.07)

4:15 p.m.

873-2 Ominous Prognostic Implications and Inadequacy of Heparin Alone for Right Heart Thrombi in Patients With Acute Pulmonary Embolism: Analysis of Baseline Characteristics, Echocardiograms, Treatment, and Clinical Outcomes in the International Cooperative Pulmonary Embolism Registry

Adam Torbicki, Samuel Z. Goldhaber, Nazzareno Galié, Anna Covezzoli, Marisa De Rosa, on behalf of the ICOPER Study Group, *Institute of Tuberculosis and Lung Disease, Warsaw, Poland.*

Background: Management of right heart thrombi (RHTh) in acute pulmonary embolism (PE) is controversial, because most reports have been small case series. Therefore, we analyzed 2, 454 consecutive acute PE patients enrolled in International Cooperative Pulmonary Embolism Registry (ICOPER).
Methods: Of the 2,454 patients, 1,143 underwent baseline echocardiography. We compared the 42 patients with versus 1,071 without RHTh.
Results: Patients with RHTh had lower systolic blood pressure (116.0±28.0 versus 125.7±25.0 mmHg, p=0.008), especially < 90 mm Hg (14% versus 5%, p=0.012), and more frequent right ventricular hypokinesis (64% versus 40%, p=0.002). However, they were similar at admission with respect to age (62.9 versus 62.5 years), arterial oxygen pressure (71.3±26.0 versus 69.5±30.5 mmHg), and prevalence of cancer (14% versus 19%). The overall mortality rate at 14 days and at 3 months was twice as high in patients with RHTh (21% versus 11%, and 29% versus 16%, respectively, p<0.05) and remained so after the exclusion of patients with right heart catheters and electrodes potentially pro-

moting local thrombogenesis (mortality at 14 days 22% versus 10%, p = 0.026). Interestingly, this difference in mortality was almost entirely observed within the subgroup of patients treated with heparin alone instead of thrombolysis or embolectomy as adjuncts to heparin (25% versus 7.2%, p=0.007), despite similar clinical severity at presentation (systolic blood pressure 122.2±24.2 versus 127.8±24.1 mmHg, hypotension in 5.9% versus 3.4%, and right ventricular hypokinesis in 52.5% versus 30.8% patients, respectively, all differences non-significant).

Conclusions: RHTh confer an ominous prognosis with increased early mortality, especially evident in patients treated with heparin alone. These findings suggest that patients with acute PE who have RHTh should be managed with more aggressive therapy than heparin anticoagulation alone, even when hemodynamically stable at the time of presentation.

4:30 p.m.

873-3 Comparison of Narrow Versus Standard Target INR Ranges

David J. Meier, Seema S. Sonnad, Julie C. Merz, William P. Fay, *University of Michigan, Ann Arbor, Michigan.*

Background: Although current guidelines suggest a target INR range of 2.0-3.0 or 2.5-3.5 for most patients, physicians frequently select narrow target INR ranges (e.g. 2.0-2.5) in an attempt to minimize complications. However, the efficacies of narrow versus standard target INR ranges are unknown. We hypothesized that narrow range management results in a greater frequency of INRs <2.0 or >4.0, which are associated with an increased risk of thrombotic and bleeding complications, respectively.

Methods: We identified 32 patients managed with both a narrow and a standard range strategy during their course of anticoagulation. Over 3000 INRs during 133 patient-years of follow-up were obtained. Sixteen patients were managed with both a 2.0-3.0 and a 2.0-2.5 range (Group A) and 16 patients were managed with both a 2.5-3.5 and a 3.0-3.5 range (Group B).

Results: Blood draws per month were more frequent (2.0±0.2 vs. 1.7±0.1; p=0.035) during narrow range management for both groups combined. For Group A, mean INR was lower (2.4±0.03 vs. 2.6±0.06; p<0.02) and frequency of INRs <2.0 was higher (23.6±2.4 vs. 17.2±2.7; p<0.04) during narrow range management. For Group B, mean INR was higher (3.4±0.03 vs. 3.1±0.06; p<0.001) and frequency of INRs >4.0 was higher (21.2±1.4 vs. 13.0±2.3; p<0.007) during narrow range management.

Conclusions: Compared to a target INR range of 2.0-3.0, management with a target range of 2.0-2.5 increases the frequency of INRs <2.0, which are associated with an increased risk of thrombotic complications. Conversely, compared to a target range of 2.5-3.5, management with a target range of 3.0-3.5 increases the frequency of INRs >4.0, which are associated with a significantly increased risk of hemorrhagic complications. Narrow target INR ranges also increase the cost and patient inconvenience associated with anticoagulant therapy. Physicians should take these issues into account before selecting narrow target INR ranges for their patients.

4:45 p.m.

873-4 Alteplase Improves the Clinical Course of Patients With Major Pulmonary Embolism: A Multicenter, Randomized, Placebo-Controlled Trial (Management Strategies and Prognosis in Pulmonary Embolism Study 3)

Stavros Konstantinides, Annette Geibel, Wolfgang Kasper, *University of Goettingen, Department of Cardiology and Pulmonary Medicine, Goettingen, Germany, St. Josefs Hospital, Wiesbaden, Germany.*

Background: The clinical benefit of thrombolytic treatment in patients with major pulmonary embolism (PE) who appear stable at presentation remains highly controversial.

Methods: In a prospective, multicenter, placebo-controlled trial, 250 consecutive patients with PE confirmed by lung scan, spiral CT, or pulmonary angiography were enrolled and 247 of them randomly assigned to treatment with alteplase (100 mg infusion over 2 h) plus heparin or heparin alone. Patients had major PE defined as 1) echocardiographic findings of right ventricular enlargement and/or pulmonary hypertension; 2) new-onset right heart strain on the ECG; or, 3) precapillary pulmonary hypertension on Swanz-Ganz catheterization. Patients with peristent arterial hypotension, cardiogenic shock, or need for cardiopulmonary resuscitation (CPR) at presentation were excluded. The primary end point was 30-day mortality or escalation/change of therapy (defined as need for breaking the code and/or one of the following: catecholamine infusion, endotracheal intubation, CPR, or emergency thrombolysis, catheter fragmentation, or surgical embolectomy) at least 2 h after randomization.

Results: Alteplase was given to 115 (47%) and heparin alone to 132 (53%) pts. No differences existed between the 2 groups with regard to the clinical symptoms, physical examination, radiologic, ECG, echocardiographic, or laboratory findings at randomization. The primary end point was reached in 31 pts (24%) of the heparin group compared with only 14 (12%) of those in the thrombolysis group (p=0.021). This difference was largely due to the more frequent need for escalation of therapy in the heparin vs. thrombolysis group (24 vs. 11%; p=0.01), since mortality was low in both groups (2 and 4 pts respectively; p=0.42). Major bleeding was 3% in the heparin and 0.9% in the alteplase group (p=0.38), whereas hemorrhagic stroke occurred in only 1 patient (0.8%) in each group.

Conclusion: In this largest to-date randomized trial of thrombolysis vs. heparin for PE, alteplase was found to favorably affect the clinical course of pts with major PE appearing hemodynamically stable at presentation, although it did not reduce in-hospital mortality.

ORAL CONTRIBUTIONS

881 Inflammation and Inflammatory Markers

Wednesday, March 20, 2002, 8:30 a.m.-10:00 a.m.
Georgia World Congress Center, Room 254W

8:30 a.m.

881-1 The Association Between Inflammatory Markers and Thrombogenic Factors in Postinfarction Patients

Tareq S. Harb, Wojciech Zareba, Arthur J. Moss, Paul M. Ridker, Nader Rifai, Victor J. Marder, Luc Miller-Watelet, *University of Rochester Medical Center, Rochester, New York.*

Background: Dyslipidemia, inflammation and thrombosis are all implicated in the pathophysiology of plaque instability and rupture. To better understand the association among these mechanisms, we investigated the relationship between levels of inflammatory markers C-reactive protein (CRP) and serum amyloid A (SAA) and thrombogenic and lipid factors in patients with established coronary artery disease.

Methods: Blood levels of CRP, SAA and various thrombogenic and lipid factors were measured 2 months after an index myocardial infarction in 957 patients. Multivariate analyses were used to determine the relationship between levels of inflammatory markers and levels of lipid and thrombogenic factors.

Results: In multivariate analysis, elevated CRP and SAA (≥75th percentile) were associated with increased levels (p<0.001) of several thrombogenic factors as summarized in the table below. Conversely, neither inflammatory marker was significantly associated with levels of lipid factors.

Conclusion: In stable post-infarction patients, there is a significant association between levels of inflammatory markers and thrombogenic factors. Conversely, levels of inflammatory markers are not significantly associated with the degree of dyslipidemia. This data suggests a possible mechanistic relationship between inflammation and thrombosis in patients with established coronary artery disease.

	Elevated CRP		*Elevated SAA*	
	OR	**CI***	**OR**	**CI***
vWF	2.21	1.50-3.25	2.79	1.88-4.14
Fibrinogen	1.013	1.011-1.016	1.010	1.008-1.012
D-Dimer	1.85	1.46-2.35	2.10	1.65-2.68

* - p<0.001
vWF - von Willebrand Factor
CI - 95% Confidence Interval
OR - Odds Ratio (expressed per 1 log unit increase in vWF and D-Dimer and per 1 mg/dl % increase in fibrinogen)

8:45 a.m.

881-2 C-Reactive Protein Predicts Microalbuminuria

Adrian W. Messerli, Ravish Sachar, Gregory L. Pearce, Byron J. Hoogwerf, Dennis L. Sprecher, *The Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Inflammation leads to endothelial dysfunction. It has been proposed that endothelial changes can lead to small losses of protein from the renal glomeruli. If C-reactive protein (CRP) is a marker for inflammation, then it may predict microalbuminuria.

Methods: We analysed serum CRP and urine albumin/ creatinine ratios (ACR) from 343 patients (n=52, diabetics) drawn from our preventive cardiology clinic. ACR values >20 mg/g were used as the cutpoint, approximating the upper quartile presented in the HOPE trial. Quintiles of CRP from our population were utilized. **Results**: Logistic regression models were constructed to determine the relative risk of microalbuminuria associated with each quintile increase in CRP. Three models were run: (1) unadjusted, (2) Framingham adjusted, and (3) Framingham + CAD status adjusted. All three models show that CRP partially explains the level of microalbuminuria for each successive CRP quintile (see table). In contrast to a previous cohort analysis, further adjustment for fibrinogen, waist, and glucose level did not change the outcome. **Conclusions**: Each progressively higher CRP quartile predicts an additional 30% risk for the presence of microalbuminuria. These data are consistent with and further substantiate the relationship between inflammation and renovascular endothelial dysfunction.

Logistic regression of RR for ACR >20 mg/g

	DM		ALL	
	OR (95% C.I)	p-value	OR (95% C.I.)	p-value
Unadjusted	2.08 (1.18-3.68)	0.01	1.38 (1.12-1.72)	0.003
Framingham Adjustment	2.06 (1.16-3.66)	0.01	1.31 (1.05 - 1.63)	0.02
Framingham + CAD	2.05 (1.15-3.67)	0.02	1.32 (1.05-1.66)	0.02